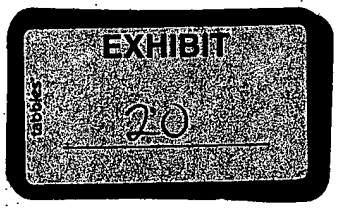

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Mediators of microvascular injury in dermal burn wounds.

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In previous studies we have demonstrated that second-degree thermal injury of skin in rats leads to secondary effects, such as systemic complement activation, C5a-mediated activation of blood neutrophils, their adhesion-molecule-guided accumulation in lung capillaries and the development of acute pulmonary injury, largely caused by neutrophil-derived toxic oxygen metabolites. In the dermal burn wound, however, pathophysiologic events are less well understood. The injury is fully developed at four hours post-burn. To further elucidate the pathogenesis of the "late phase" dermal vascular damage, rats were depleted of neutrophils or complement by pretreatment with rabbit antibody against rat neutrophils or with cobra venom factor, respectively. In other experiments, rats were treated with **blocking antibodies to IL-6, IL-1**, and TNF alpha immediately following thermal burning or were pretreated with hydroxyl radical scavengers (dimethyl sulfoxide, dimethyl thiourea). Extravasation of 125I-labeled bovine serum albumin into the burned skin was studied, as well as, skin myeloperoxidase levels. The studies revealed that, like in secondary lung injury, neutrophils and toxic oxygen metabolites, are required for full development of microvascular injury. In contrast, however, development of dermal vascular damage in thermally injured rats was not affected by complement depletion. Our data suggest that the **development of microvascular injury in the dermal burn wound is complement-independent, involves the pro-inflammatory cytokines IL-1,** TNF alpha and IL-6, and may result from reactive oxygen metabolites generated by neutrophils accumulating in the burn wound.